# MUC16 MONOCLONAL ANTIBODY AND USES THEREOF

## CROSS-REFERENCE TO RELATED APPLICATIONS

**[0001]** This application claims priority of U.S. provisional patent application filed on 62/669,058, filed May 9, 2018, the specification of which is hereby incorporated by reference in its entirety.

## BACKGROUND

### (a) Field

**[0002]** The subject matter disclosed generally relates to monoclonal antibodies against O-glycan mucin-type glycoproteins. More specifically, the subject matter relates to monoclonal antibodies against O-glycan mucin-type glycoproteins MUC16 and methods of using the same.

### (b) Related Prior Art

**[0003]** Pancreatic adenocarcinoma is the fourth-leading cause of cancer-related death in the United States with a 5 year survival rate of less than 4% and a median survival of less than 6 months. According to the American Cancer Society, the estimated number of new cases and deaths due to pancreatic cancer in the US in 2013 are 45,220 and 38,460, respectively. At the time of diagnosis more than 80% of pancreatic cancer patients have either locally advanced or highly metastatic disease.

**[0004]** Currently, Folfirinox is the first line of treatment for patients with metastatic disease and good performance status and gemcitabine alone or in combination with Abraxane is the first-line chemotherapeutic agent for the treatment of other patients with pancreatic adenocarcinoma. However, the response rate is modest, and median overall survival remains dismal. Poor patient response to chemotherapy and poor prognosis are due in part to constitutive activation of oncogenic signaling pathways that are associated with development of drug resistance, aggressive tumorigenicity and early metastasis.

**[0005]** These adverse effects result in a need for a novel molecularly targeted therapy to combat lethal cancers generally including, without limitation, pancreatic cancers.

**[0006]** It is well established that aberrant expression of membrane mucin MUC**16** is associated with tumor progression and metastasis of cancers such as ovarian and pancreatic cancer. The role of MUC16 in tumor progression and metastasis occurs through interaction with oncogenic modulators. For instance, it is understood that aberrant expression of MUC16 in ovarian cancer cells facilitates peritoneal metastasis through interactions with mesothelin (tumor differentiation factor) and through immunosuppressive functions by blocking natural killer cell-mediated cytotoxicity, while overexpression of MUC16 increases breast cancer cell proliferation via stimulation of Janus kinase 2 (JAK2). It is also understood that MUC16 is upregulated in pancreatic cancers, and expression is increased in liver metastases—although expression of MUC16 was not detected in pancreatic intraepithelial neoplasia (PanIN) nor in normal pancreas, suggesting that expression of MUC16 may occur later in disease progression.

**[0007]** Despite the role of MUC16 in disease progression being known, little is known about a possible role of oligosaccharide (O-linked glycosylation) modifications on mucin type glycoproteins. Research shows that a higher percentage of truncated O-glycan (Tn and sialyl Tn, STn) expression occurs in pancreatic adenocarcinoma, relative to other types of carcinomas, and it is well established that aberrant expression of truncated O-glycans is associated with tumour progression and adverse patient outcome. For example, STn antigen is expressed by more than 80% of human carcinomas, and in all cases the detection of STn correlates with poor prognosis and decreased overall survival of patients. Further, expression of tumour associated truncated carbohydrate antigens Tn and STn on mucin type glycoproteins are among the most common tumour-specific oligosaccharide alterations observed in adenocarcinomas. Appearance of Tn and STn epitopes on cancer cell surfaces are due to overexpression of ST6GalNAc-1 or lack of core 3 synthase/core 1 synthase activity and/or defects in Core 1 synthase specific molecular chaperone—Cosmc. Overexpression of STn antigen has been observed on many epithelial cancer cells, but the highest frequency is observed in pancreatic cancer. For example, overexpression of STn occurs early on in tumor progression on epithelial cancer cells (e.g. early epithelial benign lesions) and pancreatic cancer (e.g. pancreatic intraepithelial neoplasia stage III (PanIN-3)), which is a premalignant lesion thought to precede development of pancreatic adenocarcinoma. Altogether, these findings indicate that overexpression of truncated O-glycans is an early event leading to pancreatic cancer development. However, the exact biological mechanism of these truncated O-glycans during pancreatic tumorigenesis may not be well understood.

**[0008]** Notwithstanding over two decades of research, attempts to utilize known biomarkers of cancer, such as mucin-type O-glycan MUC16, in the development of molecularly targeted therapies for cancer have failed.

**[0009]** Therefore, there is a need for novel method for use of monoclonal antibodies that target O-glycans on mucin-type glycoproteins to inhibit activation of pro-survival cell signaling pathways.

**[0010]** Therefore, there is a need for alternative molecularly targeted therapies for targeting O-glycan mucin-type glycoprotein MUC16.

## SUMMARY

**[0011]** According to an embodiment, there is provided an antibody or an antigen-binding fragment thereof that binds to O-glycan mucin-type glycoprotein MUC16 comprising three variable heavy domain complementarity determining regions (CDR)(CDR H1, H2 and H3), and three variable light domain CDR (CDR L1, L2 and L3), wherein the CDR H1, H2, H3, L1, L2, and L3 comprise an amino acid sequence comprising:

CDR H1: (SEQ ID NO: 1)
GFTFSTF,

CDR H2: (SEQ ID NO: 2)
SSGSST,

CDR H3: (SEQ ID NO: 3)
SGYDYDPIYYALDY,